



# **Annual Surveillance Summary: *Klebsiella* Species Infections in the Military Health System (MHS), 2016**

NMCPHC-EDC-TR-406-2017

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## Abstract

The EpiData Center Department (EDC) conducts routine surveillance of *Klebsiella* species incidence and prevalence among all beneficiaries seeking care within the Military Health System (MHS). This report describes demographics, clinical characteristics, prescription practices, and antibiotic resistance patterns observed for *Klebsiella* species infections in calendar year (CY) 2016.

Multiple data sources were linked to assess descriptive and clinical factors related to *Klebsiella*. Health Level 7 (HL7)-formatted Composite Health Care System (CHCS) microbiology data identified *Klebsiella* species infections. These infections were matched to HL7-formatted CHCS pharmacy data to assess prescription practices, the Standard Inpatient Data Record (SIDR) to determine healthcare-associated exposures, Defense Manpower Data Center (DMDC) rosters to determine burden among Department of Defense (DOD) active duty (AD) service members, and the DMDC Contingency Tracking System (CTS) to determine Department of the Navy (DON) deployment-related infections.

Overall, incidence rates (IRs) of *Klebsiella* species infections in the MHS beneficiary and DOD AD populations are increasing. In 2016, the annual *Klebsiella* species IR increased by 10.8% compared to the weighted historic IR; this increase was within expected variation of *Klebsiella* species infections in the MHS populations. For severe nosocomial infections, viable treatment options are still present for *Klebsiella* species. However, for mild to moderate community-acquired infections (uncomplicated urinary tract infection), fluoroquinolones present better treatment options compared to nitrofurans based on susceptibility. Nitrofurantoin as a viable treatment option for *Klebsiella* species infections within the MHS population warrants further investigation. Diligent infection control practices, including the implementation of contact precautions, the promotion of hand hygiene adherence, and continued active surveillance, are recommended.



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## Background, Methods, and Limitations

The EpiData Center (EDC) at the Navy and Marine Corps Public Health Center (NMCPHC) prepares a retrospective report each calendar year (CY) that summarizes the demographics, clinical characteristics, prescription practices, and antibiotic susceptibility patterns for *Klebsiella* species infections among Military Health System (MHS) beneficiaries.

Literature review did not provide any new developments or research for *Klebsiella* species infections. Additionally, no new methods or limitations were applied to this annual summary. As such, this report presents analytical results and discussion of CY 2016 data for *Klebsiella* species infections in the MHS. The background, methods, and limitations relevant to this analysis have been discussed in a previous report (CY 2015 annual report for *Klebsiella*<sup>1</sup>).

The EDC also monitors other multidrug-resistant organisms (MDROs) of interest in the MHS.<sup>2,3</sup>



## Results

### Section A – Descriptive Epidemiology

#### Incidence of *Klebsiella* Species

In 2016, the annual incidence rate (IR) for *Klebsiella* species infection among MHS beneficiaries treated at a military treatment facility (MTF) was 102.1 per 100,000 persons per year. This reflects a 10.8% change above the weighted historic IR. Similar increases were demonstrated within the Air Force, Army, Navy, and Department of Defense (DOD) active duty (AD) beneficiary populations; however, a 1.3% change below the weighted historic IR was shown for the Marine Corps beneficiary population. The 2016 IRs are, however, within two standard deviations of the weighted historic IRs of *Klebsiella* species infections in the MHS, service-specific, and the Department of Defense (DOD) active duty (AD) populations (Table 1).

**Table 1.** Incidence Rate (IR) for *Klebsiella* Species Infections in the MHS, CY 2016

| Population        | 2016 IR | Weighted Historic <sup>a</sup> IR 2013 - 2015 | Two Standard Deviations: Weighted Historic <sup>a</sup> IR | 2016      |                             |
|-------------------|---------|---|--|-----------|-----------------------------|
|                   |         |   |  | Direction | Percent Change <sup>b</sup> |
| MHS Beneficiaries | 102.1   | 92.1  | 22.7   | ↑         | 10.8%                       |
| Air Force         | 92.3    | 86.3  | 20.7   | ↑         | 7.0%                        |
| Army              | 103.8   | 91.9  | 23.8   | ↑         | 13.0%                       |
| Marine Corps      | 84.0    | 85.1  | 23.3   | ↓         | 1.3%                        |
| Navy              | 96.7    | 84.3  | 19.6   | ↑         | 14.7%                       |
| DOD Active Duty   | 93.8    | 86.0  | 23.9   | ↑         | 9.0%                        |

Rates are presented as the rate per 100,000 persons per year.

A green arrow indicates an increasing percent change and a blue arrow indicates a decreasing percent change.

<sup>a</sup> Historic IR reflects the weighted average of the three years prior to the analysis year.

<sup>b</sup> This reflects the percent change from the weighted historic IR to the IR of the current analysis year.

Data Source: NMCPHC HL7-formatted CHCS microbiology and MHS M2 databases.

Prepared by the EpiData Center Department, Navy and Marine Corps Public Health Center, on 21 June 2017.



## Demographic Distribution of *Klebsiella* Species

In 2016, there were 9,605 incident *Klebsiella* species infections identified among all MHS beneficiaries treated at an MTF. The incidence rate among females (162.5 per 100,000 persons) exceeded that of males (43.9 per 100,000 persons) by nearly four times. By age, incidence rates were relatively evenly distributed across all groups with the exception of those aged 0 to 17 years, which represented the lowest burden (31.6 per 100,000 persons). By beneficiary type, retirees demonstrated the lowest rates (59.9 per 100,000 persons) (Table 2).

**Table 2.** Demographic Characteristics of *Klebsiella* Species Infections in the MHS, CY 2016

|                             | N = 9,605 |       |
|-----------------------------|-----------|-------|
|                             | Count     | Rate  |
| <b>Gender</b>               |           |       |
| Female                      | 7,498     | 162.5 |
| Male                        | 2,107     | 43.9  |
| <b>Age Group (in Years)</b> |           |       |
| 0-17                        | 618       | 31.6  |
| 18-24                       | 1,301     | 113.7 |
| 25-34                       | 1,307     | 108.8 |
| 35-44                       | 989       | 118.4 |
| 45-64                       | 2,618     | 127.5 |
| 65+                         | 2,772     | 125.0 |
| <b>Beneficiary Type</b>     |           |       |
| Active Duty                 | 1,280     | 93.8  |
| Family Members              | 6,226     | 113.8 |
| Retired                     | 1,309     | 59.9  |
| Other <sup>a</sup>          | 790       | --    |

<sup>a</sup> Rate is not reported due to variation in population denominator.

Rates are presented as the rate per 100,000 persons per year.

Data Source: NMCPHC HL7-formatted CHCS microbiology and MHS M2 databases.

Prepared by the EpiData Center Department, Navy and Marine Corps Public Health Center, on 21 June 2017.

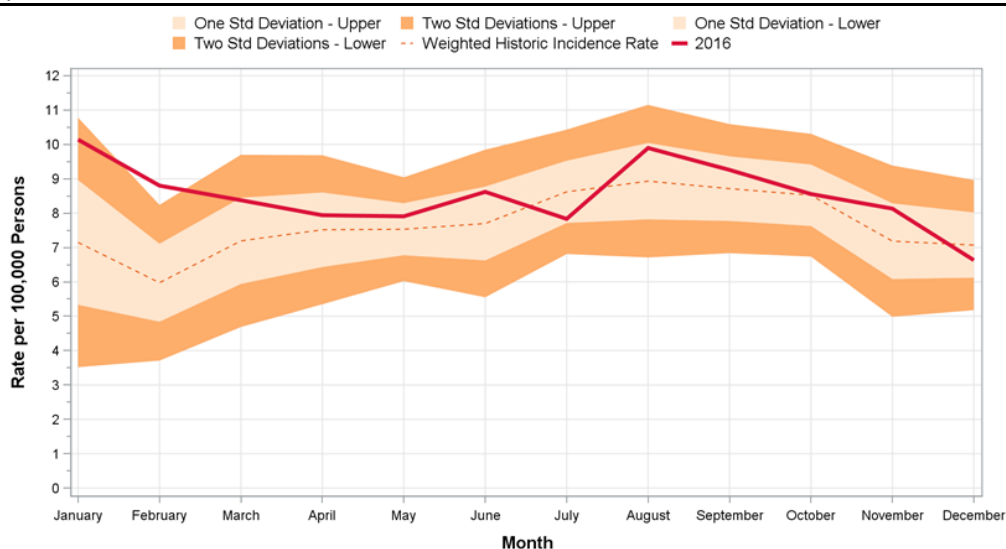




## Seasonality

Monthly incidence rates of *Klebsiella* species infections in 2016 were higher than the weighted historic IR for the majority of the calendar year and exceeded two standard deviations of the weighted historic IR in February. For the remainder of 2016, the monthly incidence rates were within two standard deviations of the weighted historic IR. The elevated rates during the first quarter of the year may be attributed to the methodology defining incidence as the first unique infection per person per calendar year. Other monthly incidence rates (July and December) for *Klebsiella* species infections were below the weighted historic monthly IR and within one standard deviation (Figure 1).

**Figure 1.** Monthly Incidence of *Klebsiella* Species Infections and Weighted Historic Incidence Rate (IR) Comparisons in the MHS, CY 2016



Rates are presented as the rate per 100,000 persons per year.

Bands indicate one and two standard deviations above and below the weighted historic monthly incidence rates (IR).

The weighted historic monthly IR is a weighted average of the three years prior to the analysis year.

Data Source: NMCPHC HL7-formatted CHCS microbiology and MHS M2 databases.

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### Klebsiella Species Clinical Characteristics

There were 10,759 prevalent *Klebsiella* species infections identified among all MHS beneficiaries treated at an MTF in 2016. The infection burden was higher in the outpatient setting (92.0%) and generally consisted of non-invasive infections (97.2%). Eighty-seven percent of *Klebsiella* species infections were collected from urine samples, while collection sites from a skin or soft tissue infection (SSTI) or wound represented the second highest proportion (5.3%). The majority of prevalent infections were caused by *K. pneumoniae* (89.6%), followed by *K. oxytoca* (8.8%) (Table 3). Invasive infections were primarily collected from blood samples (n=182; 60.7%) and respiratory samples (n=71; 23.7%) (data not shown).

**Table 3.** Clinical Characteristics of *Klebsiella* Species  
 Prevalent Infections in the MHS, CY 2016

|                                     | N = 10,759 |            |
|-------------------------------------|------------|------------|
|                                     | Count      | Percentage |
| <b>Specimen Collection Location</b> |            |            |
| Inpatient                           | 860        | 8.0        |
| Outpatient                          | 9,899      | 92.0       |
| <b>Infection Type</b>               |            |            |
| Invasive                            | 300        | 2.8        |
| Non-Invasive                        | 10,459     | 97.2       |
| <b>Body Collection Site</b>         |            |            |
| Blood                               | 183        | 1.7        |
| Respiratory                         | 336        | 3.1        |
| SSTI/Wound                          | 575        | 5.3        |
| Urine                               | 9,377      | 87.2       |
| Other                               | 288        | 2.7        |
| <b>Organism Species</b>             |            |            |
| <i>Klebsiella oxytoca</i>           | 952        | 8.8        |
| <i>Klebsiella ozaenae</i>           | 51         | 0.5        |
| <i>Klebsiella pneumoniae</i>        | 9643       | 89.6       |
| <i>Klebsiella rhinoscleromatis</i>  | 2          | 0.0        |
| <i>Klebsiella</i> species           | 111        | 1.0        |

Data Source: NMCPHC HL7-formatted CHCS microbiology database.

Prepared by the EpiData Center Department, Navy and Marine Corps Public Health Center, on 21 June 2017.



## Exposure Burden Metrics

Table 4 presents two different metrics defining MDRO infection rates for healthcare-associated exposures. In 2016, there were 239,946 direct care inpatient admissions across all MHS MTFs. The overall MDRO prevalence rate for *Klebsiella* species was 1.5 per 1,000 inpatient admissions; this metric measures the exposure of infection at any point during the admission or one year prior. The US South, US South Atlantic, and US West regions demonstrated an overall MDRO prevalence rate between 1.4 and 1.6 per 1,000 inpatient admissions. The admission MDRO prevalence rate for *Klebsiella* species was 1.3 per 1,000 inpatient admissions; this metric measures the magnitude of infection at the time of admission (importation of MDRO into the healthcare system) or one year prior. Within the US, the South Atlantic region had the highest admission MDRO prevalence rate (1.5 per 1,000 inpatient admissions) and the West region had the lowest rate (1.2 per 1,000 inpatient admissions). Among *Klebsiella* species infections, the overall MDRO prevalence rate was slightly higher than the admission MDRO prevalence rate (1.5 vs. 1.3 per 1,000 inpatient admissions); this observation suggests that the majority of MDR *Klebsiella* species infections were imported into the hospital setting from the community.

**Table 4.** MDRO Healthcare-Associated Exposure Burden Metrics among *Klebsiella* Species in the MHS, CY 2016

|                   | Overall MDRO Prevalence <sup>a</sup> |                   | Admission MDRO Prevalence <sup>b</sup> |                   |
|-------------------|--------------------------------------|-------------------|--|-------------------|
|                   | Count                                | Rate <sup>c</sup> | Count                                  | Rate <sup>c</sup> |
| <b>Region</b>     |                                      |                   |  |                   |
| OCONUS            | 21                                   | --                | 19                                     | --                |
| US Midwest        | 16                                   | --                | 16                                     | --                |
| US Northeast      | 1                                    | --                | 1                                      | --                |
| US South          | 88                                   | 1.6               | 72                                     | 1.3               |
| US South Atlantic | 126                                  | 1.6               | 117                                    | 1.5               |
| US West           | 102                                  | 1.4               | 86                                     | 1.2               |
| <b>Total</b>      | <b>354</b>                           | <b>1.5</b>        | <b>311</b>                             | <b>1.3</b>        |

<sup>a</sup> Overall MDRO prevalence included all individuals with an MDRO infection identified from a sample collected at any point during the admission, as well as samples that tested positive for infection in the prior calendar year.

<sup>b</sup> Admission MDRO prevalence included all individuals with an MDRO infection identified from samples collected up to and including the third day of admission, as well as samples that tested positive for infection in the prior calendar year.

<sup>c</sup> Rates are presented as the rate per 1,000 inpatient admissions per year.

--Rates are not provided for regions with low counts.

Data Source: NMCPHC HL7-formatted CHCS microbiology and SIDR databases.

Prepared by the EpiData Center Department, Navy and Marine Corps Public Health Center, on 21 June 2017.



## Regional Epidemiologic Infection Classifications

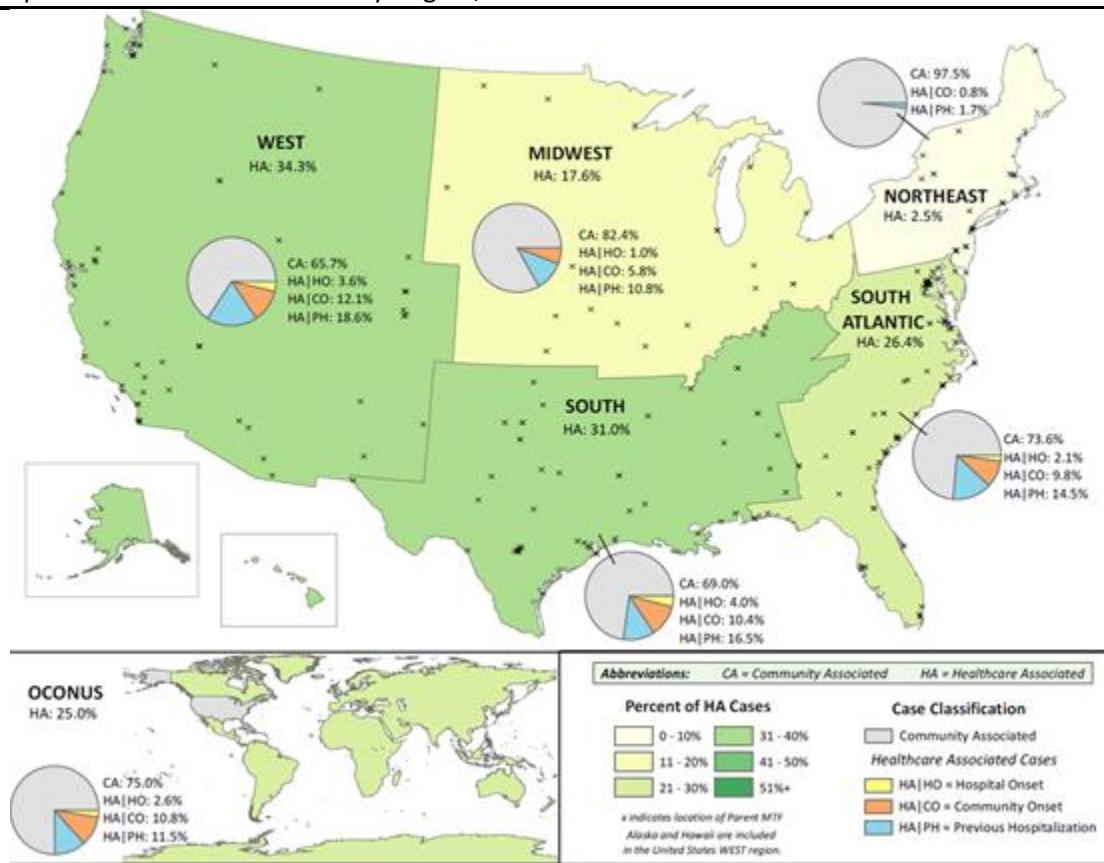
Among all prevalent *Klebsiella* species infections identified in the MHS in 2016, 71.1% were community-associated (CA) cases and 28.9% were healthcare-associated (HA) cases. Regionally, the US West reported the highest proportion of HA *Klebsiella* cases (34.3%), followed by the US South (31.0%), US South Atlantic (26.4%), OCONUS (25.0%), US Midwest, (17.6%), and the US Northeast (2.5%) (Figure 2).

HA cases were further categorized into hospital-onset (HO), community-onset (CO), or previous hospitalization (PH) groupings. Among all prevalent *Klebsiella* species infections (regardless of HA or CA classification), the greatest proportion were classified as PH cases (15.6%). Although PH cases comprised 15.6% of all prevalent *Klebsiella* species infections, the PH category accounted for 54.1% of HA cases, indicating that the *Klebsiella* species infections were not associated with a current admission but that the patient had a prior hospitalization in the previous 12 months. The second largest proportion of all prevalent infections was CO cases (10.3%), indicating that the specimens were collected within the first three days of hospital admission and the infection most likely originated from the community; CO cases encompassed 35.7% of HA cases. Only 2.9% of prevalent *Klebsiella* species infections were HO, indicating that the infection was identified after the third day of admission and likely contracted during the current hospitalization (data not shown). HO cases comprised 10.1% of the HA cases. A similar distribution of HA case classifications were observed by region, where PH cases accounted for the largest proportion, followed by CO cases and HO cases (Figure 2).

By region, previous hospitalizations represented approximately half of all HA cases in the West, South, South Atlantic, and OCONUS regions. In the Midwest and Northeast regions, previous hospitalizations accounted for almost two-thirds of all HA cases (Figure 2).



**Figure 2.** Proportion of Healthcare- and Community-Associated Cases among *Klebsiella* Species Infection in the MHS by Region, CY 2016



Data Source: NMCPHC HL7-formatted CHCS microbiology, SIDR, and MHS M2 databases.

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## Section B – Antimicrobial Resistance and Use

### Regional Multidrug Resistance

In 2016, the IR of *Klebsiella* species infection was 102.1 infections per 100,000 persons per year; the IR of drug-resistant *Klebsiella* species infection (i.e., resistant to antibiotics in at least three classes) was 7.3 infections per 100,000 persons per year. Regionally, the US West (117.6 per 100,000 persons), US South (120.6 per 100,000 persons), and US South Atlantic (114.0 per 100,000 persons) had the highest total incidence rates. The OCONUS region had a total incidence rate of 108.1 per 100,000 persons. The US Midwest and US Northeast regions accounted for the lowest total *Klebsiella* species incidence rates by region (51.6 per 100,000 persons and 17.9 per 100,000 persons, respectively) (Figure 3).

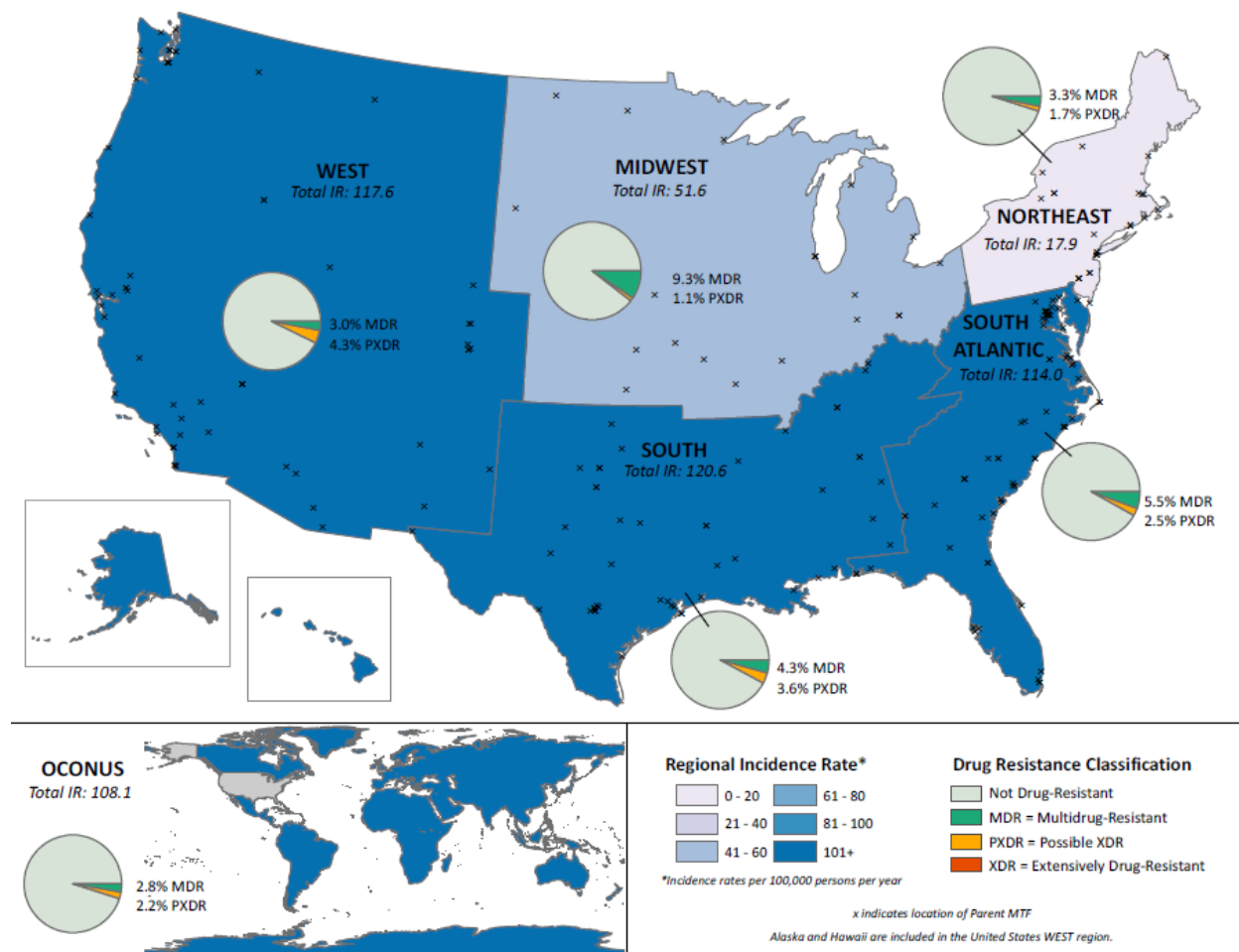
Prevalent drug-resistant *Klebsiella* species infections are further categorized by drug-resistance type; among the 829 drug-resistant prevalent infections identified during 2016, 59.0% (n=489) are classified as MDR and 41.0% as possible extensively drug-resistant (PXDR) (n=340) (data not shown). These two drug-resistant *Klebsiella* species classifications are described as a proportion of all prevalent infections by region in Figure 3. The US West accounts for the largest proportion of prevalent infections classified as PXDR (4.3%), followed by the US South (3.6%), US South Atlantic (2.5%), and OCONUS (2.2%) regions. The US Northeast (1.7%) and US Midwest (1.1%) regions account for less than two percent of prevalent infections classified as PXDR (Figure 3).

Prevalent *Klebsiella* species infections were also assessed for carbapenem resistance. Of the 10,759 prevalent infections identified among MHS beneficiaries in 2016, 0.3% (n=27) were classified as carbapenem-resistant (CR). Notably, only five CR *Klebsiella* infections were identified in 2014; however, 23 infections were identified in 2015, indicating variable counts over the past three years. The majority of CR *Klebsiella* infections during 2016 occurred among beneficiaries in the US West (n=8), followed by those in the US South Atlantic and the US South (n=7, each). Two infections were identified in each of the Midwest and OCONUS regions, and one case from the Northeast (data not shown).





**Figure 3.** Annual Incidence Rate (IR) and Percentage of Multidrug Resistance among *Klebsiella* Species Infections in the MHS by Region, CY 2016



Rates are presented as the rate per 100,000 persons per year.

Data Source: NMCPHC HL7-formatted CHCS microbiology, SIDR, and MHS M2 databases.

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## Antibiogram

Table 5 displays an antibiogram of *Klebsiella* species incident infections for all MHS beneficiaries from 2011-2016. In 2016, *Klebsiella* species infections were susceptible to a wide range of antibiotics, with susceptibility above 99% for doripenem (100.0%), ertapenem (99.7%), meropenem (99.7%), imipenem (99.2%), and amikacin (99.2%). Infections were least susceptible to ampicillin/sulbactam (85.5%) and nitrofurantoin (46.4%). Statistically significant decreases in susceptibility were observed among ampicillin/sulbactam, cefepime, cefotaxime, ceftriaxone, gentamicin, imipenem, piperacillin/tazobactam, and tobramycin, whereas significant increasing trends in susceptibility were observed in aztreonam and nitrofurantoin (Table 5).

**Table 5. Antibiogram of *Klebsiella* Species Infections Identified in the MHS, CY 2011-2016**

| Antibiotics                 | 2011 | 2012 | 2013  | 2014  | 2015  | 2016  | Susceptibility<br>Trend <sup>a</sup> | Comment <sup>b</sup> |
|-----------------------------|------|------|-------|-------|-------|-------|--------------------------------------|----------------------|
| Amikacin                    | 99.5 | 99.4 | 99.5  | 99.7  | 99.3  | 99.2  |                                      |                      |
| Amoxicillin/<br>Clavulanate | 95.9 | 96.0 | 96.4  | 96.0  | 96.5  | 95.8  |                                      |                      |
| Ampicillin/<br>Sulbactam    | 87.6 | 88.1 | 86.7  | 85.8  | 85.8  | 85.5  |                                      | ↓                    |
| Aztreonam                   | 95.8 | 95.2 | 95.6  | 97.3  | 96.8  | 97.2  |                                      | ↑                    |
| Cefepime                    | 98.1 | 98.5 | 98.6  | 98.1  | 97.8  | 97.7  |                                      | ↓                    |
| Cefotaxime                  | 98.8 | 98.2 | 98.4  | 97.7  | 98.0  | 97.6  |                                      | ↓                    |
| Cefpodoxime                 | 99.3 | 95.9 | 98.3  | 97.1  | --    | --    |                                      |                      |
| Ceftazidime                 | 97.9 | 98.4 | 98.4  | 98.3  | 98.3  | 97.9  |                                      |                      |
| Ceftriaxone                 | 97.5 | 98.2 | 98.1  | 97.7  | 97.6  | 97.3  |                                      | ↓                    |
| Cefuroxime                  | 95.2 | 94.0 | 94.4  | 94.4  | 95.0  | 94.2  |                                      |                      |
| Ciprofloxacin               | 96.9 | 97.4 | 97.5  | 97.7  | 97.5  | 97.3  |                                      |                      |
| Doripenem                   | --   | --   | 100.0 | 100.0 | 100.0 | 100.0 |                                      |                      |
| Ertapenem                   | 99.8 | 99.9 | 99.4  | 99.8  | 99.6  | 99.7  |                                      |                      |
| Fosfomycin                  | --   | --   | --    | --    | --    | --    |                                      |                      |
| Gentamicin                  | 98.6 | 98.8 | 98.6  | 98.5  | 98.4  | 98.2  |                                      | ↓                    |
| Imipenem                    | 99.5 | 99.7 | 99.4  | 99.7  | 99.4  | 99.2  |                                      | ↓                    |
| Levofloxacin                | 98.2 | 98.3 | 98.0  | 98.4  | 98.2  | 97.9  |                                      |                      |
| Meropenem                   | 99.7 | 99.4 | 99.9  | 99.8  | 99.4  | 99.7  |                                      |                      |
| Nitrofurantoin              | 42.4 | 38.7 | 37.9  | 38.0  | 41.5  | 46.4  |                                      | ↑                    |
| Piperacillin/<br>Tazobactam | 96.9 | 96.8 | 96.9  | 96.3  | 96.1  | 95.9  |                                      | ↓                    |
| Tobramycin                  | 97.7 | 98.1 | 98.2  | 97.6  | 97.7  | 97.3  |                                      | ↓                    |

'--' indicates that fewer than 30 isolates were tested.

<sup>a</sup> Susceptibility trends are displayed for antibiotics with susceptibility data for at least five consecutive years, only.

<sup>b</sup> Arrow indicates the antibiotics with a significant change in direction of trend for significant two-tailed Cochrane-Armitage tests for trend established for a single antibiotic over time. A significant increase in susceptibility is denoted by a green upward arrow and a significant decrease in susceptibility is denoted by a blue downward arrow.

Data Source: NMCPHC HL7-formatted CHCS microbiology database.

Prepared by the EpiData Center Department, Navy and Marine Corps Public Health Center, on 21 June 2017.

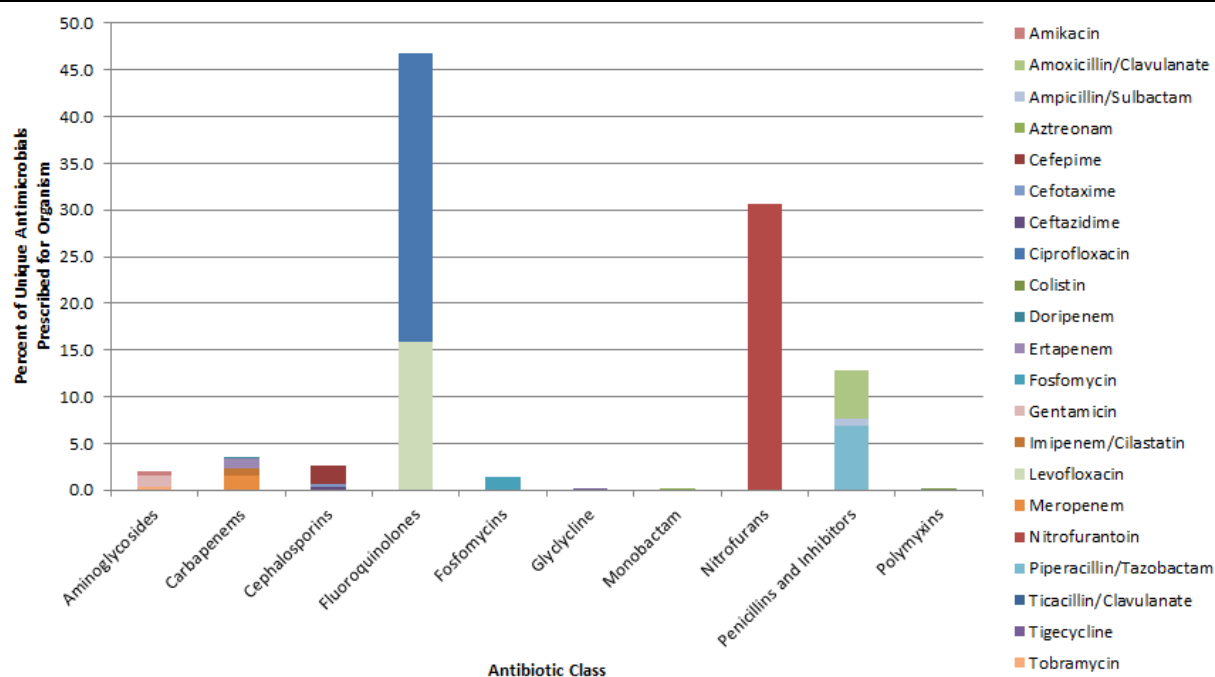




## Antimicrobial Consumption/Prescription Practices

Among all MHS beneficiaries, the most commonly prescribed antibiotic classes associated with *Klebsiella* species infections in 2016 were fluoroquinolones (46.8%), nitrofurans (30.6%), and penicillins and inhibitors (12.8%) (Figure 4). Within the fluoroquinolone class, ciprofloxacin (30.9%) and levofloxacin (15.9%) were prescribed. Among penicillins and inhibitors, piperacillin/tazobactam (6.8%), amoxicillin/clavulanate (5.1%), and ampicillin/sulbactam (0.8%) were prescribed (Figure 4).

**Figure 4. *Klebsiella* Species Infection and Prescription Practices in the MHS, CY 2016**



Only the first occurrence of a unique antibiotic was counted per person per infection, regardless of administration route.

Data Source: NMCPHC HL7-formatted CHCS microbiology and HL7-formatted pharmacy databases.

Prepared by the EpiData Center Department, Navy and Marine Corps Public Health Center, on 21 June 2017.

## Section C – Special Populations

Of the 10,759 prevalent *Klebsiella* species infections in 2016, less than 1% (N = 21) occurred among Department of the Navy (DON) AD deployed personnel. Of these deployment-related *Klebsiella* species infections, 66.7% (n=14) were female and 33.3% (n=7) were male. All DON AD deployment-related infections occurred among service members aged 18-44, with 52.4% (n=11) occurring among those aged 25-34.



## Discussion

This report describes an increase in *Klebsiella* species infection rates, from the weighted historic IR of 92.1 infections per 100,000 persons from 2013-2015 to 102.1 infections per 100,000 persons in 2016. When compared to weighted historic IRs, percent increases in the incidence rates of *Klebsiella* species infections were observed among beneficiaries from all service branches, with the exception of the Marine Corps, which saw a percent decrease of 1.3%.

Assessment of clinical and demographic characteristics found that urinary tract infections (UTIs) were the most common manifestation of *Klebsiella* species infections, and rates were highest among women. These results are consistent with other literature citing *Klebsiella* species as the agent for 6-15% of all inpatient and outpatient UTIs, and women are significantly more likely to experience a UTI than men.<sup>4,5</sup> The IRs of *Klebsiella* species infections were distributed relatively evenly throughout all age groups, with the exception of beneficiaries less than 17 years of age who accounted for the lowest rate. The presence of infection in the 0-17 age category is not without consideration. UTIs in children can cause long-term medical sequelae, requiring prompt diagnosis and management to prevent subsequent complications.<sup>6</sup>

*Klebsiella* species infections classified as either MDR or PXDR occurred far less frequently than other *Klebsiella* species infections, where the multidrug-resistant proportion was approximately one-thirteenth of the total *Klebsiella* species prevalence. The US West, US South, and US South Atlantic regions accounted for the top three regional incidence rates of all infections; however, the US Midwest, US South Atlantic, and US South had the highest proportion of multidrug-resistance among prevalent *Klebsiella* species infections ranging from 4.3-9.3%.

Analyses defining MDRO healthcare-associated exposure burden metrics implicate community acquisition of drug-resistant *Klebsiella* species across each region. A large proportion of MDR *Klebsiella* species infections were imported into the healthcare system; the admissions prevalence rate during 2016 (1.3 per 1,000 inpatient admissions) accounted for approximately 87% of the overall prevalence rate (1.5 per 1,000 inpatient admissions). With the exception of the US Northeast, elevated MDRO prevalence admissions rates were observed across all regions. These results underscore the need for drug-resistance surveillance outside of traditional hospital settings as well as the diligent use of infection control practices, including the implementation of contact precautions, the promotion of hand hygiene adherence, and continued active surveillance within the healthcare setting.<sup>7</sup>

*Klebsiella* species isolates retained high susceptibilities to many tested antibiotics, indicating a range of viable treatment options for infections. Except for two antimicrobials (ampicillin/sulbactam and nitrofurantoin), *Klebsiella* species isolates displayed susceptibilities upwards of 94% to all tested antibiotics. When compared to 2015 antibiogram results, six additional antibiotics displayed significant decreases in susceptibility over the surveillance period. Although nitrofurantoin accounted for one of two antimicrobials that significantly increased in susceptibility over the surveillance period, it maintained the lowest susceptibility in 2016. These results are noteworthy, as analyses also identified a large proportion of nitrofurantoin prescriptions during 2016 for treatment. Further assessments may be warranted to



describe the occurrence of nitrofurantoin treatment followed by another recommended regimen for *Klebsiella* species infections, as some physicians could be empirically treating for UTIs thought to be caused by *Escherichia coli*, which accounts for roughly 80% of CA UTIs.<sup>8,9</sup> Ciprofloxacin and levofloxacin represent two additional antimicrobials most prescribed for *Klebsiella* species infections in this assessment, which are also recommended as oral doses by Johns Hopkins for mild to moderate, community-acquired infection of uncomplicated UTIs, or as intravenous regimens for severe, nosocomial infections without the risk of methicillin-resistant *Staphylococcus aureus*.<sup>10</sup>

In summary, this report documents a continued, upward trend for *Klebsiella* species infection rates among MHS beneficiaries first noted in 2014. The characteristics of these infections during 2016 are concurrent with existing literature, which reports a higher burden among females and predominant clinical presentation as UTIs. Almost three-quarters of infections were classified as CA cases, underscoring the need for research and surveillance assessing *Klebsiella* species as a community-acquired infection. Furthermore, the elevated MDRO admission metrics indicate a higher magnitude of MDR *Klebsiella* species imported into the MHS, as opposed to an existing reservoir of infection in the healthcare setting. Finally, these results indicate viable treatment options are still present for *Klebsiella* species infections; however, nitrofurantoin as a possible treatment option, despite percent susceptibility in the forties, warrants further investigation.

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## Appendix A: Antibiotics List

**Table A1.** Antibiotics Included in the Resistance Definitions for *Klebsiella* spp. in the DOD, CY 2016

| Antibiotic Class   | Antibiotics Included in Class |
|--|-------------------------------|
| Aminoglycosides  | Amikacin                      |
|  | Gentamicin                    |
|  | Netilmicin                    |
|  | Tobramycin                    |
| Anti-MRSA Cephalosporins <sup>a</sup>                                      | Ceftaroline                   |
| Antipseudomonal penicillins and $\beta$ -lactamase inhibitors              | Piperacillin/Tazobactam       |
|  | Ticarcillin/Clavulanic Acid   |
| Carbapenems  | Doripenem                     |
|  | Ertapenem                     |
|  | Imipenem                      |
|  | Meropenem                     |
| 1st & 2nd Generation Cephalosporins (non-extended spectrum cephalosporins) | Cefazolin                     |
|  | Cefuroxime                    |
| 3rd & 4th Generation Cephalosporins (extended spectrum cephalosporins)     | Cefotaxime or ceftriaxone     |
|  | Ceftazidime                   |
|  | Cefepime                      |
| Cephameycins   | Cefoxitin                     |
|  | Cefotetan                     |
| Fluoroquinolones   | Ciprofloxacin                 |
|  | Levofloxacin                  |
| Folate pathway inhibitors  | Trimethoprim/Sulfamethoxazole |
| Fosfomycins  | Fosfomycin                    |
| Glycylcyclines   | Tigecycline                   |
| Monobactam   | Aztreonam                     |
| Penicillins & $\beta$ -lactamase inhibitors                                | Amoxicillin/Clavulanic Acid   |
|  | Ampicillin/Sulbactam          |
| Phenicol   | Chloramphenicol               |
| Polymyxins   | Colistin                      |
| Tetracyclines  | Doxycycline                   |
|  | Minocycline                   |
|  | Tetracycline                  |

<sup>a</sup> Included only for *Klebsiella pneumoniae* and *K. oxytoca*.

Source: Magiorakos et al., 2012.<sup>11</sup>

Prepared by the EpiData Center Department, Navy and Marine Corps Public Health Center, on 21 June 2017.





## Appendix B: Acronym and Abbreviation List

| Acronym/Abbreviation | Definition  |
|----------------------|---|
| AD                   | active duty   |
| CA                   | community-associated  |
| CHCS                 | Composite Health Care System  |
| CO                   | community-onset   |
| CONUS                | continental United States   |
| CR                   | carbapenem-resistant  |
| CTS                  | Contingency Tracking System   |
| CY                   | calendar year   |
| DMDC                 | Defense Manpower Data Center  |
| DOD                  | Department of Defense   |
| DON                  | Department of the Navy  |
| EDC                  | EpiData Center Department   |
| HA                   | healthcare-associated   |
| HL7                  | Health Level 7 format   |
| HO                   | hospital-onset  |
| M2                   | Military Health System (MHS) Management Analysis and Reporting Tool |
| MDR                  | multidrug-resistant   |
| MDRO                 | multidrug-resistant organism  |
| MHS                  | Military Health System  |
| MTF                  | military treatment facility   |
| NMCPHC               | Navy and Marine Corps Public Health Center                          |
| OCONUS               | outside the continental United States                               |
| PXDR                 | possible extensively drug-resistant                                 |
| PH                   | previous hospitalization  |
| SIDR                 | Standard Inpatient Data Record                                      |
| US                   | United States   |
| UTI                  | urinary tract infection   |

